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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/705,197	11/12/2003	Elena Babiychuk	58764.000039	3003

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EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 05/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/705,197	BABIYCHUK ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *November 12, 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0304*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims require an RNA molecule comprising a sense nucleotide sequence comprising an nucleotide sequence of about 100 consecutive nucleotides from a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID No 1, the nucleotide sequence of SEQ ID No 3. the nucleotide sequence of SEQ ID No 5, or the nucleotide sequence of SEQ ID No 10; and ii) an antisense nucleotide sequence comprising a nucleotide sequence of about 100 consecutive nucleotides from the complement of a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID No 1, the nucleotide sequence of SEQ ID No 3, the nucleotide sequence of SEQ ID No 5 or the nucleotide sequence of SEQ ID No 10.

A sense nucleotide sequence comprising a nucleotide sequence "of about 100" consecutive nucleotides from a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID No 1, the nucleotide sequence of SEQ ID No 3. the nucleotide sequence of SEQ ID No 5, or the nucleotide sequence of SEQ ID No 10 does

not find support in the specification as filed and thus constitutes new matter. An antisense nucleotide sequence comprising a nucleotide sequence "of about 100" consecutive nucleotides from the complement of a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID No 1, the nucleotide sequence of SEQ ID No 3, the nucleotide sequence of SEQ ID No 5 or the nucleotide sequence of SEQ ID No 10 also does not find support in the specification as filed and thus constitutes new matter.

Claims 36-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method for obtaining high vigor in a plant cell when compared to a control plant cell, comprising introducing a chimeric gene in said plant cell to yield a transgenic cell, wherein said chimeric gene comprises the following operably linked DNA regions: a) a plant-expressible promoter; b) a DNA region, which when transcribed yields a RNA molecule, said RNA molecule being capable of reducing the expression of endogenous PARP genes; and c) a DNA region involved in transcription termination and polyadenylation wherein said RNA molecule comprises a sense nucleotide sequence comprising an nucleotide sequence of about 100 consecutive nucleotides from a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID No 1, the nucleotide sequence of SEQ ID No 3. the

nucleotide sequence of SEQ ID No 5, or the nucleotide sequence of SEQ ID No 10; and ii) an antisense nucleotide sequence comprising a nucleotide sequence of about 100 consecutive nucleotides from the complement of a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID No 1, the nucleotide sequence of SEQ ID No 3, the nucleotide sequence of SEQ ID No 5 or the nucleotide sequence of SEQ ID No 10; said sense nucleotide sequence and said antisense nucleotide sequence being capable of combining into a double stranded RNA region; and wherein said vigor of said plant can be measured by measuring the capacity of explants of said plant to reduce 2,3,5-triphenyltetrazoliumchloride. The claims are also drawn to a transgenic plant and seed, and to a chimeric gene.

The specification at page 52 discloses that for *Arabidopsis thaliana* and *Brassica napus* plants comprising combinations (APP/ZAP) of PCD modulating genes under the control of a CaMV35S or NOS promoter, a high vigor is observed in a number of the transgenic lines. The specification at pages 43-44 discloses two types of PCD modulating genes under the control of a CaMV35S or NOS promoter, dsRNA-ZAP, disclosed as comprising a DNA region comprising i) a sense nucleotide sequence comprising a ZAP encoding DNA region (about complete) (the *Arabidopsis thaliana* homologue to SEQ ID NO:10, isolated by hybridization), and ii) an antisense nucleotide sequence comprising about 500 base pairs of the 5' end of the ZAP2 encoding DNA region (SEQ ID NO:10), and dsRNA-APP, disclosed as comprising a DNA region comprising i) a sense nucleotide sequence comprising an APP encoding DNA region (about complete) (SEQ ID NO:5), and ii) an antisense nucleotide sequence comprising about 500 base pairs of the 5' end of the APP encoding DNA region (SEQ ID NO:5).

With respect to dsRNA-ZAP, the specification does not disclose the specific nucleotide sequence of the sense nucleotide sequence comprising a ZAP encoding DNA region (about complete) (the *Arabidopsis thaliana* homologue to SEQ ID NO:10, isolated by hybridization), or the specific nucleotide sequence of an antisense nucleotide sequence comprising about 500 base pairs of the 5' end of the ZAP2 encoding DNA region (SEQ ID NO:10). With respect to dsRNA-APP, the specification does not disclose the specific nucleotide sequence of a sense nucleotide sequence comprising an APP encoding DNA region (about complete) (SEQ ID NO:5), or the specific nucleotide sequence of an antisense nucleotide sequence comprising about 500 base pairs of the 5' end of the APP encoding DNA region (SEQ ID NO:5).

The claimed invention is not enabled because making and using double stranded RNA molecules that can produce a specific phenotype in a particular type of plant cell is unpredictable, as the ability of a double stranded RNA molecule to suppress gene expression and produce a specific phenotype in a plant cell depends on multiple variables which include but are not limited to the length of the RNA molecule and its composition relative to the target gene, and the degree of homology between the RNA molecule and the intended target gene and other genes in the plant cell.

See, for example, Fire A. et al. (Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*. Nature. 1998 Feb 19;391(6669):806-11), who teach that injection into *C. elegans* of double stranded RNA corresponding to the 5' part of the *C. elegans unc-54* gene results in a lethal phenotype, whereas injection of double stranded RNA corresponding to other parts of the gene results in a paralysis phenotype (Table 1 page 807).

See also, for example, Bosher J.M. et al. (RNA interference can target pre-mRNA: consequences for gene expression in a *Caenorhabditis elegans* operon. Genetics. 1999 Nov;153(3):1245-56), who teach that injection into *C. elegans* of double stranded RNA corresponding to the full length *C. elegans lir-1* gene results in an embryonic arrest phenotype, whereas injection of double stranded RNA corresponding to smaller stretches of *lir-1* exonic sequences resulted in a varied array of phenotypes (page 1247 column 2 last paragraph through page 1247 column 1 first paragraph; page 1249 Figure 3; page 1250 Figure 4).

See additionally, for example, Wang M.B. et al. (Application of gene silencing in plants. Curr Opin Plant Biol. 2002 Apr;5(2):146-50. Review), who teach that in plants, introns seem to be poor targets for posttranscriptional silencing, and that silencing appears to be most efficient when sequences of more than 300 base pairs are used to target hpRNA constructs (page 147 column 1).

See further, for example, Helliwell C. et al. (Constructs and methods for high-throughput gene silencing in plants. Methods. 2003 Aug;30(4):289-95), who teach that a lower frequency of gene silencing is obtained when shorter gene fragments are used in hpRNA constructs, but that longer gene fragments increase the chance of recombination (page 293 column 2). Helliwell C. et al. also teach that the effectiveness of silencing appears to be gene dependent (page 293 column 2). Helliwell C. et al. further teach that since the mechanism of silencing depends on sequence homology, there is potential for cross-silencing of related mRNA sequences (page 293 column 2).

In the instant case the specification does not provide sufficient guidance with respect to which of the recited RNA molecules to express, and in what type of plant cell,

to produce a plant cell that has a high vigor phenotype. Absent such guidance one skilled in the art would have to make a variety of different chimeric genes which when transcribed yield the types of RNA molecules encompassed by the claims, and then test each chimeric gene for its effect on plant cell vigor, in order to discriminate between those chimeric genes which when transcribed yield RNA molecules that function as claimed and those chimeric genes that do not. Such a trial and error approach to practicing the claimed invention would constitute undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36-39, 44-48 and 52, and claims dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 36-39, 44-48 and 52 are indefinite in the recitation of "of about 100". It is unclear how many consecutive nucleotides the nucleotide sequence can consist of, as the specification does not explicitly or implicitly define the quantity "of about 100", and the quantity cannot be determined from other limitations recited in the rejected claims.

Remarks

No claim is allowed.

Claims 36-53 are deemed free of the prior art due to the failure of the prior art to teach or suggest a chimeric gene comprising the following operably linked DNA regions: a) a plant-expressible promoter; b) a DNA region, which when transcribed yields a RNA

molecule, said RNA molecule being capable of reducing the expression of endogenous PARP genes; and c) a DNA region involved in transcription termination and polyadenylation wherein said RNA molecule comprises a sense nucleotide sequence comprising an nucleotide sequence of about 100 consecutive nucleotides from a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID No 1, the nucleotide sequence of SEQ ID No 3. the nucleotide sequence of SEQ ID No 5, or the nucleotide sequence of SEQ ID No 10; and ii) an antisense nucleotide sequence comprising a nucleotide sequence of about 100 consecutive nucleotides from the complement of a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID No 1, the nucleotide sequence of SEQ ID No 3, the nucleotide sequence of SEQ ID No 5 or the nucleotide sequence of SEQ ID No 10; said sense nucleotide sequence and said antisense nucleotide sequence being capable of combining into a double stranded RNA region.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins
Primary Examiner
Art Unit 1638

CC

5/11/06